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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/802,644 | 03/09/2001 | Jeff W. Lichtman | WSHU 2010.1 | 8528 |

321 7590 03/04/2003

SENNIGER POWERS LEAVITT AND ROEDEL
ONE METROPOLITAN SQUARE
16TH FLOOR
ST LOUIS, MO 63102

EXAMINER

WEBER, JON P

ART UNIT

PAPER NUMBER

1651

DATE MAILED: 03/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/802,644

Applicant(s)

LICHTMAN ET AL.

Examiner

Jon P Weber, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 06 December 2002.

2a) ☒ This action is **FINAL**.

2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-45 is/are pending in the application.

4a) Of the above claim(s) 20-33 and 37-40 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-19, 34-36 and 41-45 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.

4) ☐ Interview Summary (PTO-413) Paper No(s). _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

Status of the Claims

The response with amendments filed 06 December 2003 has been received and entered. Claims 1-45 have been presented for examination.

Election/Restrictions

This application contains claims 20-33 and 37-40 drawn to an invention nonelected with traverse in Paper No. Paper No. 7, filed 30 May 2002 and withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group. A **complete** reply to the final rejection **must** include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 103

Claims 1-19 and newly added 41-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haugland et al. (US 5,436,134) and Yue (US 5,656,449) in view of Magrassi et al. (1987), Gan et al. (1999) and Gee et al. (US 5,888,829) and further in view of Pichersky (US 5,849,526) and Sanford et al. (US 4,945,050).

It is argued that Haugland et al. (US 5,436,134) and Yue (US 5,656,449) disclose metal particles as the microparticle, or particularly, ferrite crystals, gold or tungsten. It is urged that Haugland et al. (US 5,436,134) and Yue (US 5,656,449) do not exemplify a biolistic process for introducing dyes. It is argued that Magrassi et al. (1987) do not disclose lipophilic dyes. It is urged that none of Magrassi et al. (1987), Gan et al. (1999) and Gee et al. (US 5,888,829) or Pichersky (US 5,849,526) disclose dye coated metal particles. It is argued that Dellaporta (US

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6,013,486), although not relied upon, but mentioned as duplicative of the teachings of Pichersky (US 5,849,526) only applies to administering DNA even though they do indicate that the particles can be metal particles such as ferrite crystals, gold or tungsten. It is urged that there is no motivation to combine the references.

The response is in error that the dyes of Magrassi et al. (1987) are not lipophilic. In evidence are provided the following: Wissing et al. (2002), see page 37747, column 2, paragraph 2, "Because AO is a **lipophilic** weak base, it is readily membrane-permeable and can accumulate in acidic compartments ..."; Davey et al., see paragraph bridging pages 2-3, "It is well documented that the mitochondria of eukaryotic cells have the ability to concentrate "**lipophilic**" cations such as rhodamine 123 ..."; Sigma-Aldrich Catalog, see pages 3-4, "**Lipophilic** and membrane probes" wherein are listed many dimethylamino styryl pyridium salts. Hence the majority of the dyes listed in Magrassi et al. (1987) are demonstrated to be lipophilic. The mere fact that the dyes are cationic is not a basis for their not being lipophilic.

While Haugland et al. (US 5,436,134) and Yue (US 5,656,449) do not exemplify a biolistic process for introducing dyes coated onto microparticles, they clearly contemplate this method as one of several functionally equivalent methods. The advantages of one method of introducing the dyes over another are not discussed. Haugland et al. (US 5,436,134) and Yue (US 5,656,449) do not explicitly describe what the microparticles may be made of. However, it was well-known in the art that biolistic processes used microparticles composed of inert substances such as ferrite crystals, gold or tungsten as evidenced by Dellaporta (US 6,013,486) and noted in the response. One can consider the several patents granted to Sanford and associates

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that are of record, wherein these kinds of metal nanoparticles are disclosed to be particularly well suited to a biolistic process.

As representative, Sanford et al. (US 4,945,050) is cited. At column 6, lines 39-44, the inert particles may be ferrite crystals, gold or tungsten spheres. The particles may be coated with any biological or substance that can be freeze dried, coated onto, or bonded to the particles (column 6, lines 55-65). Particularly, the biological substance can include biological stains such as fluorescent or radiolabeled probes, including proteins such as enzymes, DNA or RNA *inter alia* (column 7, lines 8-13).

Hence, it would be *prima facie* obvious to any person of ordinary skill in the art to select metal particles for such a biolistic process from among the many possible nanoparticles. Presumably Haugland et al. (US 5,436,134) and Yue (US 5,656,449) thought it was so well established that it was unnecessary to recite the specific materials in the nanoparticles. There is no reason why a person of ordinary skill in the art would expect that the biolistic process was limited to coating the particles with nucleic acids as instantly argued, especially in view of the teachings of Sanford et al. (US 4,945,050).

Claims 34-3⁶~~8~~ and newly added 45 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al. (1998; ref 32) in view of Tsien (1998) and Matz et al. (1999) and further in view of Sanford et al. (US 4,945,050).

It is argued that none of Wong et al. (1998; ref 32) in view of Tsien (1998) or Matz et al. (1999) teach metal particles.

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As discussed above, Sanford et al. (US 4,945,050) establishes that the inert particles in the biolistic process are preferably inert particles such as ferrite crystals, gold or tungsten spheres, especially when involving DNA or RNA encoding a protein.

Hence, it would be *prima facie* obvious to select metal particles such as ferrite crystals, gold or tungsten spheres as the biolistic particles for introducing DNA or RNA encoding a fluorescent protein because these are the preferred materials for such a process.

Applicant's arguments filed 06 December 2002 have been fully considered but they are not persuasive. The rejections under 35 U.S.C. 103 are adhered to for the reasons of record and the additional reasons above.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

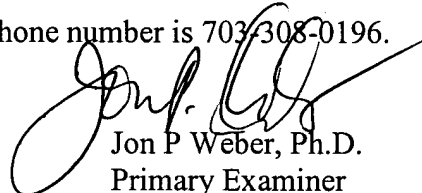
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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Jon P Weber, Ph.D.
Primary Examiner
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JPW
February 27, 2003